

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C. 20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 20 December 1999 (20.12.99)	
International application No. PCT/US99/07546	Applicant's or agent's file reference DALHO1270WO
International filing date (day/month/year) 06 April 1999 (06.04.99)	Priority date (day/month/year) 06 April 1998 (06.04.98)
Applicant GOODWIN, Avery et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

05 November 1999 (05.11.99)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

S. Mafla

Telephone No.: (41-22) 338.83.38

P. ENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 24 JUL 2000

WIPO

PCT

Applicant's or agent's file reference DALHO1270WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/07546	International filing date (day/month/year) 06 APRIL 1999	Priority date (day/month/year) 06 APRIL 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant DALHOUSIE UNIVERSITY		

1. This international preliminary examination report has been prepared by the International Preliminary Examining Authority and is transmitted to the applicant according to Article 3.

2. This REPORT consists of a total of 5 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 05 NOVEMBER 1999	Date of completion of this report 29 JUNE 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer <i>Dorothy Lawrence Fox</i> ANNE L. HOLLERAN
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/07546

I. Basis of the report**1. With regard to the elements of the international application:***

- ☒ the international application as originally filed
- ☒ the description:
pages 1-24 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____
- ☒ the claims:
pages 25-31 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____
- ☒ the drawings:
pages 1-2 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____
- ☒ the sequence listing part of the description:
pages 1-2 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in printed form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages None
- ☒ the claims, Nos. None
- ☒ the drawings, sheets/fig None

5. ☒ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/07546

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. statement**

Novelty (N)	Claims <u>1-18 and 24-33</u>	YES
	Claims <u>19-23 and 34-37</u>	NO
Inventive Step (IS)	Claims <u>1-18 and 24-33</u>	YES
	Claims <u>19-23 and 34-37</u>	NO
Industrial Applicability (IA)	Claims <u>1-37</u>	YES
	Claims <u>None</u>	NO

2. citations and explanations (Rule 70.7)

Claims 19-23 lack novelty under PCT Article 33(2) as being anticipated by Tomb et al (Tomb, J-F. et al., Nature, 388: 539-547, 07 August 1997.).

Claims 19-23 are interpreted as claims to nucleic acids encoding a nitroreductase of *H. pylori* and to nucleic acids of 19 and 20 which have been transfected into host cells for the purpose of recombinant expression. The phrases "encoding" and "having" allow a broad interpretation of the boundaries of the claimed nucleic acids. Thus, the claimed nucleic acids may include regions encoding for other proteins of *H. pylori*.

Tomb et al disclose the entire genomic sequence of *H. pylori* and thus disclose the nucleic acids of claims 19 and 20. Tomb et al also disclose methods for determining open reading frames (page 547) and discuss the importance of *H. pylori* as a human pathogen (page 539). Recombinant methods of nucleic acid expression are well known, especially as a tool to further characterize an encoded protein. Also the structure of the nucleic acids of claims 19 and 20 does not substantially change when placed into a heterotypic cell. Thus, the teachings of Tomb et al suggest the nucleic acids of claims 19 and 20 and the uses of them in claims 21-23.

Claims 34-37 lack novelty under PCT Article 33(2) as being anticipated by Townson et al (Townson, S.M. et al., Acta. Tropica, 56: 173-194, 1994).

Claims 34-37 are drawn to kits for identifying bacteria which express a nitroreductase comprising substrates for nitroreductases. The novelty of the claimed kits rests in the novelty of the substrates. However, the claims are broadly drawn to kits comprising any substrate of a nitroreductase and also specifically to a kit comprising metronidazole.

Townson et al teach nitroheterocyclic drugs such as metronidazole (see page 173 and also abstract) which (Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

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VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 18 and 31 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): claim 18 is missing a phrase such as "converting a" after the phrase "capable of" and claim 31 is missing the antecedent for "said carrier".

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/07546

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): A61K 39/395, 31/04, 31/05, 31/06; C12N 1/21, 9/06, 11/02; C07H 21/04 and US Cl.: 424/ 178.1; 435/177, 178, 179, 181, 182, 188, 189, 191, 252.3; 514/579, 646, 740, 742; 536/ 23.7

I. BASIS OF REPORT:

5. (Some) amendments are considered to go beyond the disclosure as filed:

NONE

V: 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

demonstrates that substrates making up the claimed kits are not novel over the prior art.

Claims 1-18 and 24-33 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the conjugates, nitroreductases, pharmaceutical formulations and methods for killing or inhibiting growth of cells, methods of detecting plasmid loss and methods of identifying substrates.

NEW CITATIONS

NONE

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/07546

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : Please See Extra Sheet.

US CL : Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/ 178.1; 435/177, 178, 179, 181, 182, 188, 189, 191, 252.3; 514/579, 646, 740, 742; 536/ 23.7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,633,158 A (ANLEZARK et al) 27 May 1997, see entire document.	1-17, 24-31
X,P	GOODWIN et al. Metronidazole resistance in <i>Helicobacter pylori</i> is due to null mutations in a gene (rdxA) that encodes an oxygen-insensitive NADPH nitroreductase. Molecular Microbiology. April 1998, Vol. 28, No. 2, pages 383-393, see entire document.	18,19
Y,P		1-17, 24-31
X	TOWNSON et al. Resistance to the nitroheterocyclic drugs. Acta Tropica. March 1994, Vol. 56, No. 2-3, pages 173-194, see entire document.	34-37
Y		8-10, 26, 27



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
B earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Z* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

30 JUNE 1999

Date of mailing of the international search report

11 AUG 1999

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

NANCY A. JOHNSON

Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/07546

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X - Y	TOMB et al. The complete genome sequence of the gastric pathogen <i>Helicobacter pylori</i> . Nature. 07 August 1997, Vol. 388, pages 539-547, see entire document.	20-22 --- 23
X - Y	Database GENBANK, Accession No. AE000604, AE000511, TOMB, J-F. et al. <i>Helicobacter pylori</i> 26695 section 82 of 134 of the complete genome. 06 August 1997.	20-22 --- 23
A	LEVINSON et al. Medical Microbiology and Immunology. Norwalk, Connecticut: Appleton and Lange. 1994, pages 98-99.	14,15
Y	US 5,387,598 A (ROSSIGNOL) 07 February 1995, column 1, lines 25-45 and column 7, line 66 - column 8, line 39.	11, 34-37
Y	WO 97/02020 A1 (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH) 23 January 1997, pages 15-18.	12, 34-37

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/07546

A. CLASSIFICATION OF SUBJECT MATTER:

IPC (6):

A61K 39/395, 31/04, 31/05, 31/06; C12N 1/21, 9/06, 11/02; C07H 21/04

A. CLASSIFICATION OF SUBJECT MATTER:

US CL :

424/ 178.1; 435/177, 178, 179, 181, 182, 188, 189, 191, 252.3; 514/579, 646, 740, 742; 536/ 23.7

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, MEDLINE, EMBASE, BIOSIS, CAPLUS

search terms: nitroreductase, helicobacter, conjugate, pyrrole, furans, thiophene, imidazole, oxazole, thiazole, pyrazole, pyridine, pyrimidine, purine, quinoline, isoquinoline, carbazole, nitazoxanide, nitrofurazone